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Neck Residue of Nasopharyngeal Carcinoma (NPC): Timing of Diagnosis and Treatment

Ferucha Moulanda*, Marlinda Adham

Department of Otorhinolaryngology Head and Neck Surgery, Faculty of Medicine Universitas Indonesia-Cipto Mangunkusumo General Hospital, Jakarta, Indonesia

Abstract

Introduction: Prognosis of patients with NPC has improved but the risk of persistence regional of disease is still a critical problem. Timing of diagnosis the condition along with immediate yet appropriate treatment should be considered.
Case report: Female 35 year-old diagnosed with NPC T2N3M0 and had finished neo-adjuvant chemotherapy (NAC) continued with chemoradiation (CRT) from July until December 2020. Clinical follow up on January 2021 showed palpable and fixated lymph node at level V of right neck sized 3x3x2.5 yet no mass identified at nasopharynx area. Patient was clinically diagnosed as neck residue of NPC and further management choices between early neck dissections or adjuvant chemotherapy (AdjCT) was still debatable in the multidisciplinary team discussion.
Conclusion: Neck residue diagnosis for high risk features of NPC should be made early. Immediate appropriate treatment should be considered since its associated with prognosis and overall survival of NPC patient.

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Corresponding author:
Address: A Staff Building, 7th Floor. Jl. Pangeran Diponegoro No.71, Kec Senen, Jakarta Pusat, 10430, Indonesia

e-mail: drferuchamoulanda@gmail.com

1. CASE REPORT

NPC is still one of the most frequent head and neck cancer in our center. Result of comprehensive treatment in nasopharyngeal carcinoma (NPC) have improved recently due to the awareness of the clinicians, advances imaging modality, radiotherapy techniques, and combined treatments approach. Intensity-modulated radiotherapy (IMRT) is preferred currently for NPC because excellent locoregional control can be managed by this radiation technique. However, small proportion of residual lymph nodes patients were still identified after complete treatment, ranging from 3.5% to 6.9% and regional recurrence can happen in 7%-16% patients [1, 2]. Residual lymph node was defined when the malignant masses in neck nodes do not regress completely by 3 months after completion of comprehensive treatment [3]. Patient usually came for follow up during one month and then 3 months after completion of CRT for Magnetic Resonance imaging (MRI) evaluation. Early diagnosis of neck residue is important for arranging the next step of treatment.

A 35-year-old female referred from ancillary hospital with chief complaint lump at the left neck and behind the ear area that getting bigger for 3 months prior to admission. There was history of left ear fullness along with ringing ear since one month ago. There were no history of nasal blockage, headache nor double vision. Patient was a housewife with no history of smoking nor excessive consumption of salted fish. From physical examination of neck showed enlargement of bilateral level II, III and V lymph nodes, fixated with smooth surfaces with largest size 6x5x3 cm at the left neck (level II and III). Endoscopic examination of nasopharynx showed mass at the posterolateral wall obliterated left Rosenmuller fossa and torus tubarius. Biopsy of this mass showed the undifferentiated non-keratinized squamous cell carcinoma (WHO type III). MRI showed suspicious malignant nasopharyngeal mass with extension to the left parapharyngeal space, carotid space, left lateralis pterygoid muscle, multiple bilateral lymphadenopathy with biggest size 5.8x6.9x2.7 cm. No distant metastases were found in metastatic workout.

Picture 1. Image of neck nodes prior to NAC and CRT

Patient was diagnosed with T2N3M0 NPC and scheduled for NAC then continued with CRT (66 Gy of RT) from July 2020 until December 2020. Patient was coming for follow up to Oncology ENT clinic on January 2021. Nasopharynx endoscopy examination showed thickened posterior wall with no mass appearance, Rosenmuller fossa and torus tubarius were clearly identified. Neck examination showed enlargement and fixated level V right lymph node sized 3x2x2 cm with smooth surface. Karnofsky performance score was 80-90. Dry mouth was experienced after CRT; however patient was still able to eat and drink properly. MRI follow up was scheduled on March 2021. Decision made by multidisciplinary team (cancer team) meeting was to observe/wait and see until the MRI result comes out ensuring the locoregional residue.

Picture 2. Image of neck nodes after NAC and CRT.

2. DISCUSSION

Timing of diagnosis and appropriate course of treatment of residual lymph nodes for NPC can be challenging. The National Comprehensive Cancer Network (NCCN) guidelines recommend neck dissection for these cases however neck dissection alone is probably insufficient and perhaps need more intensive treatment methods such as chemotherapy [4]. Adjuvant chemotherapy (AdjCT) post RT is also considered a potential approach to reduce distant failures and can start early after CRT with several consideration related patient choices and risk of toxicity [5].

Although NPC is a radiosensitive cancer, evidently the residual lymph nodes may not be or less sensitive to radiotherapy and lead to the increase potential of recurrence and distant metastasis [1]. The node control rate was about 70% in N2 and N3 patients, but increase around 90% with N0 and N1 disease. The surrounding tissue and structures had been changed and injured by the first radiation which usually cannot tolerate re-irradiation [6]. The change in neck area also can mimic residual nodes and need to be assessed with caution [7]. This patient came in the first month duration after completion of CRT. Nasopharynx endoscopic examination and clinical neck examination were routinely performed in our center accordance to the multidisciplinary guideline published by Simo et.al though histologically the response in NPC believe to complete up to three months [7].

Neck residue in this case was found at level V of right neck. The lymph drainage order will be changed and irregular theoretically, because of the lymphatic system of the neck was destroyed by radiation therefor tumor would tend to expand in situ [8]. Previous study showed that cancer-bearing lymph node in level II and V were usually isolated, and cases with positive level III or level IV lymph node mostly had the ahead levels involved [9]. Cohort study by Wang et al. [10] showed that highest nodal metastasis site was found at level II (79.7%) meanwhile Wei et al. [6] mostly found the residue lymph nodes in level II and V. Size of the residue neck in this case was half of the diagnostic size and found in early follow up. Most of the guidelines were recommended to wait until 3 months after the completion of CRT. Meanwhile several studies showed that persistence neck nodes demonstrated locally aggressive behavior with a high incidence of extracapsular extension (54-56%), affecting non-lymphatic tissue (35%) and extended near to the spinal accessory nerve (28%) [6].

In this case, the patient was diagnosed earlier with N3 and included as high-risk features. Other high risk features reported by Liu et al. [5] that included as high risk criteria were: (1) size of neck node > 6 cm; (2) involvement of supraclavicular node; (3) skull base destruction/intracranial invasion with multiple nodes metastasis; or (4) multiple neck nodes metastasis with one of nodal size> 4 cm. Liang et al. [11] also reported that higher T and N stage relevant with poorer prognosis meanwhile Feng et al.[12] reported the important implication of necrosis lymph node that could increase the chance for bigger radioresistence of hypoxic tumor then lead to residue cases. Xu et al.[13] studied that AdjCT was mostly benefit for N3 NPC patients. It usually started 3 months after completion CRT based on consideration of the Intergroup study 0099 that reported poor compliance rate of AdjCT around 50–60% when it started 1 month after RT and not strong enough to tolerate immediate regimen AdjCT with significant toxicities effect [6]. Chen et al.[14] reported several multicenter studies showed around 60%-70% of total patients was able to tolerate the entire regimen AdjCT if started 1 month after CRT. Zhang et al.[15] studied that oral AdjCT with S-1 can started in 3 weeks after completion CRT with complete response found in 77.3% cases meanwhile total incidence of severe acute toxicities was 9.1%, the incidence and extent of mucositis and late adverse reaction were tolerable.

Study by Tsang et al. [2] showed that neck dissection was superior in controlling nodal failures than reirradiation. Neck dissection also considered due to the tendency of highly malignant, invasive and high ECS incidence to the non-lymphatic structure in neck residue [8]. The overall survival reported by Yeung et al.[16] was about 56.5% (mean follow-up of 45.3 months) with mild and moderate (nearly 10%) surgical complication which can be cured conservatively, while regional recurrence free survival was 91.3%. Risk stratification might be obtained from neck dissection specimen after salvage surgery in residual or recurrent NPC. The practical threshold were if absolute number of positive lymph nodes found more than 5 and lymph node density more than 20% [16]. Data studied by Wang et al.[3] demonstrates additional prognostic factors which were the size of residual or recurrent lymph node metastasis, level V lymph node involvement, surgical procedure performed and distant metastasis.

The extensive salvage surgery was recommended when the recurrent lymph nodes diagnosed in more than one level or the size was very large or immovable. Selective neck dissection (SND) should be performed with recommendation to dissect level II–III when the level III was involved, the level II–IV should be dissected if level IV were positive, the entire involved level should be dissected if the lymph node only found in level I or II or V. The lymph node resection (LNR) were proven to be effective if the lymph node was isolated and/or movable and/or with diameter less than 3 cm [9].

Similar to the management of other head and neck primary tumors, the timing and indication for salvage neck dissection after CRT has been a topic of debate. Usually based on the guideline, evaluation will be performed after 12 weeks of treatment completion and wait and see will be conducted during patient's follow up. Nevertheless, we think that the treatment plan should be settled up early when the diagnosis firstly made mainly for the high-risk features with risk of residue. Early diagnosis of persistence disease in high-risk NPC after completion of treatment should be made shortly when clinical follow up performed and additional treatment should be urgently scheduled. AdjCT can be a choice if patient have a good Karnofsky performance score meanwhile waiting for the 12 weeks MRI follow up. However, if the toxicity of previous CRT is intolerable and considered the local aggressive behavior of residue NPC, we suggest to perform incisional biopsy with frozen section then followed with neck dissection if positive cancer cell was positive. Neck dissection procedure should be followed by AdjCT for the better prognosis and overall survival. As for this case, due to the high-risk characteristic existed since early diagnose confirmed and strongly suspected large neck residue found after 1 month of NAC and CRT completion, we will prefer to perform incisional biopsy procedure in general anesthesia then directly proceed with selective right neck dissection if positive cancer cell found by frozen section examination and continued with AdjCT. Systemic morbidity due to the previous NAC and CRT could be worsened if only relied on chemotherapy without being preceded by surgical procedure to remove the mass, thus we prefer to proceed with AdjCT after selective neck dissection. Further future research about efficacy and overall survival of early scheduled neck dissection (less than 3 months after CRT) will be needed.

3. CONCLUSION

Diagnosis of neck residue NPC should be made early. More attention should be given to the high-risk features patient and immediate treatment choices must be discussed with the patient and multidisciplinary team (MDT), however personalized treatment option should also be considered by the clinician for a better overall survival.

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